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| EXAMINER | |
|---|---|
| WESSENDORF, TERESA D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | |

| NOTIFICATION DATE | DELIVERY MODE |
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| 07/05/2007 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/540,392 | MARKUS, BEIER | |
| | Examiner | Art Unit | |
| | T. D. Wessendorf | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *2,3,13 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

***Election/Restrictions***

Applicant's election of Group I, (claims 4-12 and 14-16) in the reply filed on 5/14/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's election of the species, nucleic acid receptor is likewise acknowledged. Further, in the telephonic interview on May 2, 2007 with applicant's representative Robert Murray, biotin was elected as the species for hapten. (Please note that since claim 4 depends on claim 1 hence, claim 1 would be examined together with the elected group I).

Claims 2-3, 13 and 17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/14/2007.

***Status of Claims***

Claims 1-17 are pending

Claims 2-3, 13 and 17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species.

Claims 1, 4-12 and 14-16 are under examination.

***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-12 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1 is unclear whether the synthesis in the carrier is carried out with a single basic unit of each of the polymer receptors in a passing liquid or a polymer is contained in a liquid that is immobilized on the carrier. It is not clear how the zones are predetermined such that a specific block

immobilizes to a specific zones to enable synthesis of the desired polymer. There seems to be a lack of essential steps/elements in the process steps. Also, it is unclear as to when the immobilization is alternatively or simultaneously done such that it is site and/or time specific. It is not clear as to the process step(s) included in the term "characterized". This last rejection has the same import for claims 4-12 and 14-16.

2. Claim 4 is unclear as to when it is "preferable" to use a closed channel(s). This rejection has the same import in claim 7, "particularly preferably".

3. Regarding claim 5 the phrase "such as" and "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

4. The term "high-affinity" in claim 8 is a relative term which renders the claim indefinite. The term "high" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

5. Claims 10 and 11 are unclear as to the steps encompassed by the application of the hapten groups in a planar or site-specific **fashion**. It is not clear as to the differentiating

steps of applying the hapten to the carrier as recited in claims 10-12.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 5-7 and 10-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Edman et al (USP 6780584).

Edman discloses at col. 50, line 35 up to col. 51, line 23:

..Combinatorial synthesis of biopolymers such as oligonucleotides and peptides at reaction zone test sites. A significant advantage of the combinatorial synthesis disclosed in this invention allows very large numbers of sequences to be synthesized on a device (dependent on the number of SPM microlocations). Key to this is the employment of those devices having either individual buffer chamber(s) for each test site or individual control and modulation of the electric field at each reaction zone. The basic concept for combinatorial synthesis capitalizes on the use free field electrophoretic transport to deliver, concentrate, and react monomers, coupling reagents or deblocking reagents at specific addressable microlocations on the device. Alternatively, the electric field can be utilized to protect sites from reaction.

One method for combinatorial oligonucleotide synthesis begins with a set of selectively addressable microlocations whose surfaces have been derivatized with blocked primary amine (X--NH--) groups (the specific binding entity). The initial step in the process involves selective deblocking of microlocations using a charged deblocking reagent (the first charged entity). In this case, the reagent would carry a positive (+) charge and would be present in the common first chamber. The process is carried out by applying a negative bias to the second (lower) chamber electrodes specific to individual test site microlocations. Conditions would be chosen to rapidly concentrate the deblocking agent at the specific test sites to a level necessary to achieve rapid and selective deblocking of the desired functional group. In short, application of positive (or in other cases, negative) potentials to selective electrodes causes the charged reagents to be moved from a reagent delivery site or chamber and concentrated at the desired microlocation being de-blocked.

In the second step, chemical coupling of the first base, to the deblocked microlocations is carried out by simply exposing the system to the phosphoramidite reagent (x-base) in the upper chamber. The nucleotide couples to de-blocked entities at the selected microlocations, but not to any of the blocked entities at other microlocations. At this point, standard phosphoramidite chemistry is carried out until the next de-blocking step.

> At the second de-blocking step, those electrodes specific to the desired microlocations which are to be coupled with the next base are made negative, as above, and those to be protected are not activated. The system is now exposed to the next base to be coupled, and selective coupling to the de-blocked microlocation is achieved, as above. The coupling and de-blocking procedures are repeated, until all the different DNA sequences have been synthesized at each of the test site microlocations.

Edman discloses at e.g., col. 36, lines 24-25 the synthesis in the device of antibody-antigen interactions involving large or small antigen-hapten. See further the details of the method in the Examples, col. 55 up to col. 60.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-12 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edman in view of Hiller et al (USP 20050101031) and Lowery et al (20060172335).

Edman is discussed above. Edman does not disclose a microfluidic channel and a hapten attached to the substrate. However, Lowery discloses at Example 6:

> [0203] Alternatively, and equally preferred is where the reaction receptacle comprises a fluidic channel, and preferably, a microfluidic channel. As used herein, the term microfluidic refers to a channel or other conduit that has at least one cross-sectional dimension in the range of from about 1 micron to about 500 micron. Examples of microfluidic devices useful for practicing the methods described herein include, e.g., those described in e.g., U.S. Pat. Nos. 5,942,443, 5,779,868, and International Patent Application No. WO 98/46438, the disclosures of which are incorporated herein by reference.
>
> [0204] ..by using a microfluidics platform, it may be possible to mimic the compartmentalization of a eukaryotic cell. This method could then be used to monitor the activity of group transfer reactions catalyzed by enzymes in a more native environment, in the context of other proteins and with cellular components that may affect enzymatic activity. Therefore, data on the activity of enzymes that catalyze group transfer reactions and the consequences of their inhibition can be obtained in a setting that will more accurately reflect an in vivo environment.
>
> [0206] Movement of materials through the channels of these microfluidic channel networks is typically carried out using any of a variety of known techniques, including electrokinetic material movement (e.g., as described in U.S. Pat. No. 5,858,195 (fully incorporated by reference), pressure based flow, axial flow, gravity flow, or hybrids of any of these.

Hiller et al discloses at paragraph [0068] haptens that are immobilized as allergens on the microarray chip. A "hapten" is a low molecular weight (typically weighing less than about 7000 Daltons) substance that is generally incapable of causing, by

itself, a significant production of antibodies upon administration to an animal body, including a human body. By providing haptens which are immobilized to the microarray chip a higher density can be achieved on the chip. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a microfluidic channel in the method of Edman as taught by Lowery. Lowery teaches that the use of microfluidic e.g., mimics the compartmentalization of a eukaryotic cell which would provide the motivation to use microfluidic in the method of Edman. Likewise, the benefits obtained in the use of hapten in a microarray (carrier, as claimed) in the method of Edman that results in a higher density on the chip as taught by Hiller would provide the motivation to attach a hapten in the carrier. (Edman also suggests the use of a hapten).

No claim is allowed.

## ***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Ramsing et al (USP 20060147924) discloses that oligonucleotides have even been used as building blocks in

nanotechnology applications to make molecular structures with a defined geometry (cubes, cylinders etc.).

2. Skrzypcznski, Zbigniev, et al (USP 20040073017) discloses synthesis of monomer blocks.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0765. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
June 22, 2007